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TITLE: Crozer-Chester Medical Center Burn Research Projects

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14. ABSTRACT
The Nathan Speare Regional Burn Treatment Center is under contract with the U.S. Army Institute for Surgical Research in conjunction with the Army Burn Center to carry out two studies under protocols established by Army researchers. Study 1 is "Automated Fluid Resuscitation of Burn Patients". Study 2 is "Evaluation of Aquacel Ag".

Screening and enrollment continues for Studies 1 and 2. Five (5) patients were enrolled in Study 1 with 2 patients completing the 48 hours in the study. The strict inclusion criteria continued to be an issue with enrollment. The Crozer IRB required consent IN PERSON. After discussing the issue with the IRB several times, they agreed to allow us to obtain phone consent. We plan to request a 2 year extension to allow completion of the study. Thirteen (13) patients were enrolled in Study #2 with 9 completing the full study course. We are nearing completion of this study. Two burn staff nurses became research certified and were educated on the process of obtaining consent and set-up of the fluid resuscitation equipment to assist the research team in times of need.

15. SUBJECT TERMS
Automated fluid resuscitation devices, Closed-Loop algorithms, Kramer resuscitation; Aquacel Ag Dressing, Donor site care

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Crozer-Chester Medical Center Nathan Speare Regional Burn Treatment Center

ANNUAL REPORT TO THE U.S. ARMY INSTITUTE OF SURGICAL RESEARCH FOR THE PERIOD 7/19/2011 to 7/18/2012 (Year 5)

Title: "Crozer-Chester Medical Center Burn Research Projects"

Contract Number: W81XWH-07-1-0311, as amended

INTRODUCTION:

The purpose of the proposed project is to conduct burn research that will benefit combat casualties in the current conflict. The Army Burn Center, which is part of the Brooke Army Medical Center in Fort Sam Houston, Texas, has demonstrated the applicability of burn research in civilian populations to combat populations. The Nathan Speare Regional Burn Treatment Center is under contract with the U. S. Army Institute for Surgical Research to carry out two projects according to protocols that have been already established by Army researchers. A third project has been defined by Crozer's Principal Investigator. These projects are:

Study 1: "Automated Fluid Resuscitation of Burn Patients"
The purpose of Study 1 is to collect data which will be used to create an effective resuscitation algorithm for the development of a closed loop resuscitation system. The actual use of the closed loop resuscitation system will occur in a future study. Approximately 40 patients will be enrolled. The project is expected to improve resuscitation of burn patients by creating a feedback loop of actual patient response to resuscitation volumes, and titrating the fluid therapy to changes in urinary output. Data from urimeters, cardiac monitors and IV pumps will be measured at 10-minute intervals and fed to a DAQ, which is a computer system designed to collect data from this equipment at the bedside.

Study 2: "Evaluation of Aquacel Ag Dressing for Autogenous Skin Donor Sites"
This study will compare the performance of an agreed upon dressing to the normal standard of care (Xeroform). Patients who are scheduled for excision and split thickness skin grafting of burns will have one of two donor sites covered with the Aquacel Ag dressing, and the other treated according to standard care. Approximately 30 patients will be enrolled. The hypothesis is that mean healing time for wounds treated with Aquacel Ag dressing will be less than the mean healing time for wounds treated with Xeroform dressing. Specific aims are: 1) that pain as perceived by the patient will be equal to or less than with the Aquacel Ag dressing as compared with the standard dressing, and 2) the cosmetic effect of healing at post surgery day 30-45 will be equal or less with the Aquacel Ag dressing as compared with the standard of care dressing.

Study 3: A Comparison of Clinical and Microbiological Efficacy of Three Separate Antibiotic Regimens Against *Acinetobacter baumannii*.
A. baumannii has been steadily emerging as a poly-resistant organism in burn treatment centers. In addition to the problem of widespread colonization of patient care areas, there has been the progressive development of multiple resistance genes. The goal of this project is to evaluate the microbiological and clinical efficacy of three potential antimicrobial agents over 24-months in

three groups of 20 adult patients with documented *A. baumannii* infections to determine if there are any subtle or frank differences in outcome with the use of these antimicrobials. Using standard manufacturer-recommended doses, we intend to compare two agents that have not been routinely used, colistin and tigacycline, to imipenem-cilistatin to guide best practices in *A. baumannii* treatment. Using standard statistical testing methods the duration of treatment, time to onset of infection, and other parameters will be investigated. Standard assessment of infection response will be used to evaluate and compare these three agents. Pilot data on Crozer burn patients with *A. baumannii* pneumonia will also be analyzed.

BODY:

The approved Statement of Work is as follows:

Study 1, Protocol Title: "Automated Fluid Resuscitation of Burn Patients – Phase 1"

Task 1: To collect data from 40 study subjects which will be used to create an effective resuscitation algorithm for the development of a closed loop resuscitation system.

a. Complete project start-up activities (hiring and training of research staff, purchasing equipment) (Year 1, Quarter 1)
b. Enroll 15 study subjects and collect data (Year 1, Quarters 2-4)
c. Enroll 5 study subjects and collect data (Year 2, Quarter 1)

Study 2, Protocol Title: "Evaluation of Aquacel Ag for Autogenous Skin Donor Sites"

Task 1: Enroll up to 30 patients in this multi-center trial to evaluate the performance of the identified dressing versus standard of care dressing (Xeroform) for skin donor sites in terms of day of healing, comfort, cosmetics and ease of use.

a. Complete project start-up activities (hiring and training of research staff) (Year 1, Quarter 1)
b. Enroll 75% of study subjects, harvest subject's donor sites, randomize dressing to donor sites, and conduct clinical assessments (Year 1, Quarter 2-4)
c. Enroll 25% of study subjects, harvest subject's donor sites, randomize dressing to donor sites, and conduct clinical assessments (Year 2, Quarter 1)
d. Summarize results (Year 2, Quarter 1)

Study 3, Protocol Title: "A Comparison of Clinical and Microbiological Efficacy of Three Antibiotic Regimens Against *Acinetobacter baumannii*"

Task 1: To collect data from three groups of 40 patients and to compare the responses to antibiotic therapy with specific focus on: 1) differences in duration of therapy; 2) differences in time to eradication of infection (laboratory findings changes, vital signs, culture results); 3) differences in adverse reaction profiles of the patients; and 4) impact on the susceptibility of *A. baumannii* to these agents over a two year period.

a. Complete project start-up activities (hiring and training research staff) (year 1, quarter 1)
b. Enroll 45 subjects and collect data (year 1, quarters 2-4)
c. Enroll 15 subjects and collect data (year 2, quarters 1)
d. Enroll 60 additional subjects (year 2, quarters 2-4, Year 3, quarter 1)
e. Compose report, submit abstract for national meeting presentation, write manuscript for publication (year 4, quarter 2)

(Note: 'd' and 'e' will extend beyond the grant period. See Proposal Narrative)

Discussion

Study 1 (Resuscitation Study)

We continue to screen every admission on a 24/7 basis with on-call coverage of the research team. During FY 2011-2012, a total of 512 patients were screened. 22 patients had a TBSA ≥ 20%. 5 patients were enrolled. 2 patients completed the full 48 hours on the study. 3 patients did not complete the full 48 hours. 1-transferred to another hospital, 1-needed emergent CT scan and 1-computer malfunction occurred. The other 17 patients with ≥ 20% TBSA were excluded for a variety of reasons: 2-unable to obtain consent, 5-age, 4-didn't require CVC and/or foley, 2-went to OR within first 24 hours after injury, and 5-other.

On 5/18/2012, a computer and IV pump malfunction occurred during data collection on a patient and data may have been compromised. Several attempts were made at communicating with the Army computer engineer without success. As of 6/18/2012, there has been no response. There is a second computer and 2 other IV pumps to use until the others are repaired.

The strict inclusion criteria continued to be an issue with enrollment. The Crozer IRB required consent IN PERSON. After discussing the issue with the IRB several times, they agreed to allow us to obtain phone consent.

2 burn staff nurses became research certified and were educated on the process of obtaining consent and set-up of the fluid resuscitation equipment. This was done to cover the resuscitation study when no other research staff was available (ABA). A summary of patients screened and entering the study during the annual report period is shown in the table below.

AUTOMATED FLUID RESUSCITATION STUDY - MONTHLY SUMMARY

JUL 2011-JUN 2012	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	TOTAL	STUDY TOTAL
# SCREENED	52	57	33	32	26	42	47	39	37	43	53	51	512	752
# <20% BSA	48	54	31	31	25	42	46	35	36	41	51	50	490	719
# <18 YEARS OLD	13	16	7	6	4	9	11	8	5	12	9	12	112	166
# NON-BURN	4	2	4	3	3	4	9	5	7	2	7	9	59	81
# >20% BSA	4	3	2	1	1	0	1	4	1	2	2	1	22	33
# INCLUDED IN STUDY	0	2	1	0	1	0	0	0	0	0	1	0	5	7
# EXCLUDED	52	55	32	32	25	42	47	39	37	43	52	51	507	745
DATE LAST UPDATED	7/31/2011	8/31/2011	9/30/2011	10/31/2011	11/292011	1/3/2012	2/6/2012	3/1/2012	4/2/2012	5/2/2012	6/4/2012	7/2/2012		
Notes - see below	1	2	3	4	5		6	7	8	9	10	11		

Note 1: 1 pt qualified, but no one in family spoke or read English. Pt vented. 2nd pt excluded due to age. 3rd pt with road rash excluded. 4th pt was admitted >24hrs post-burn.

Note 2: 1st Pt 25% TBSA, but didn't require central line. 2nd pt agreed to be in study and signed consent, but couldn't tolerate foley. 3rd pt enrolled & completed approx 44 hrs on DAQ before being tranferred to another burn center.

Note 3: 1 pt 53%, but was 17 y/o

Note 4: 1 pt excluded due to extensive psych hx, no CVC and no foley.

Note 5: Enrolled pt was only on DAQ for 2-3 hrs. Needed to be disconnected for stat CT scan.

Note 6: 1 pt 69%, but family was making pt DNR. Pt expired within 36 hrs of admit. 2nd pt was ?19-22%. Resident documented 22%. Attending documented 19%. Went with attending's assessment of 19%.

Note 7: 2 Pts had approx 30% TBSA, but were <18 yrs old. 3rd pt was 65.5% TBSA, but no immed. family was available to give consent within 24 hr time frame. 4th pt was 29% TBSA, but was taken to the OR within first 24hrs.

Note 8: 1 pt 22% TBSA, but went straight to the OR for escharot. immed upon admission. 2nd pt was calculated as 18% on admit & 26% the next day, but after the 24 hr time frame.

Note 9: 1st pt 41%, but excluded due to age (3 y/o). 2nd pt 21%, but research staff was not notified that pt admitted.

Note 10: 1 pt enrolled but computer malfunc. Collected maybe 24 hrs of data. 2nd pt didn't require central line until after the 24 hr time frame.

Note 11: 1 pt had TBSA 24.5%, but did not require CVC or foley within 24 hr time frame.

Study 2 (Donor Site Study)

Enrollment continues. A total of 512 patients were screened during FY 2011-2012. 13 patients were enrolled and 9 completed the study. Of the 4 who did not complete the study, 1-removed by research staff due to problems with the Aquacel Ag site (patient was still followed for the full course), 1-did not come to follow-up appointments, 1-enrolled prior to viewing wounds and wounds were only 78cm^2, and 1-didn't receive STSG in OR, just excision and VAC placement.

For the entire study period, a total of 30 patients have been enrolled. 23 patients have completed the study. In reviewing the paperwork, there are 3 patient charts that have too much data missing and will potentially be excluded and there are 4 patients that were withdrawn by research staff. We determined that a total of 7 patients will need to be replaced to meet the requirements of the study. To date 1 of these patients has been replaced, leaving 6 patients left to enroll. A summary of patients screened and entering the study is shown in the table below.

RESEARCH MONTHLY SUMMARY - DONOR SITE STUDY - AQUACEL AG

JUL 11-JUN 12	JUL	AUG	SEP	OCT	NOV	DEC	JAN	FEB	MAR	APR	MAY	JUN	TOTAL	STUDY TOTAL
# PATIENTS SCREENED	52	57	33	32	26	42	47	39	37	43	53	51	512	1603
# MEETING CRITERIA	3	0	3	1	0	2	1	0	1	1	1	2	15	56
# EXCLUDED	49	57	31	31	26	40	46	39	36	43	53	49	490	1561
# ENROLLED IN STUDY	3	0	2	1	0	2	1	0	1	0	1	2	13	30
# COMPLETING STUDY	3	0	0	1	0	1	1	0	1	0	0	2	9	23
# DECLINED	0	0	1	0	0	0	0	0	0	0	0	0	1	16
# PTS <18 YEARS OLD	13	16	7	6	4	9	11	8	5	12	9	12	112	166
# NON-BURN PTS	4	2	4	3	3	4	9	5	7	2	7	9	59	81
DATE LAST UPDATED	7/31/2011	8/31/2011	9/30/2011	10/31/2011	11/29/2011	1/3/2012	2/6/2012	3/1/2012	4/2/2012	5/2/2012	6/4/2012	7/2/2012		
Notes - see below	1	2	3			4				5	6			

Note 1: 3 pts currently enrolled and are expected to complete study in next 1-2 weeks

Note 2: 2 pts with extensive psych hx excluded. 2 pt w/ road rash excluded. 1 pt missed. Was not aware pt was going to OR.

Note 3: 2 pts enrolled. 1 removed from study on POD #6 due issues w/ Aquacell site. Pt was followed until healed in outpt clinic. 1 pt was no call, no show for 3 outpt appts. Unable to obtain photos 30-45 days post-op.

Note 4: 1 pt enrolled. Unable to view wounds prior to OR. Wounds assessed in OR. Found to be 78cm2. Too small for study.

Note 5: 1 pt qualified, but was taken to OR before research staff knew of pt

Note 6: Pt scheduled for STSG and enrolled. Did not receive STSG in OR, just excision and VAC. Pt removed from study.

Study 3: Study 3, a project defined by Crozer, has not begun because Crozer has not had any patients that met the criteria for inclusion since April, 2008. The study was focused on the poly-resistant *A. Baumannii*, which was eliminated in the burn unit in 2007 and has not recurred. In order to fully utilize the burn research nurse, we have worked on other projects applicable to the military theatre which have contributed to other areas of burn research. In the Annual Report period, we completed the following activities:

Current Projects/Presentations/Publications

Current IRB-Approved Projects

- Risk versus Benefit of the Addition of Acetaminophen to Oxycodone for Pain Management at the Nathan Speare Regional Burn Treatment Center

- Retrospective review of the experience of the Nathan Speare Regional Burn Treatment Center use of cultured epithelial autografts (CEA) in patients with massive burn injuries

- Central Venous Catheter Exchange Strategies in Patients with Acute Burn Injury at Nathan Speare Regional Burn Treatment Center

- Comparison of instilled versus nebulized aminoglycosides in the treatment of tracheobronchitis associated with persisting endotracheal intubation in thermal injury patients

- Calciphylaxis Management in a Burn Treatment Center

- Stevens - Johnson Syndrome and Toxic Epidermal Necrolysis Management in a Burn Treatment Center

- Transfusion triggers in burn patients-a retrospective review

Oral Presentation-ABA 2012

An open, prospective randomized pilot investigation evaluating pain with the use of soft silicone wound contact layer, Mepitel® One, vs. Bridal Veil and staples used on split thickness skin grafts as a primary dressing.

Presented by Dr Patton (coordinating investigator), et al with Molnlycke® Healthcare

Poster Presentations-ABA 2012

- Management of purpura fulminans in a burn treatment center
- Pyoderma gangrenosum in a burn treatment center
- Trimethoprim-induced hyperkalemia in burn admission treated with intravenous or oral trimethoprim sulfamethoxazole
- Impact of multiple drug resistant (MDR) *Acinetobacter baumannii* on changes in antibiotic susceptibility of *Pseudomonas aeruginosa* **(Won best in category)**

Poster Presentation-SCCM 2012

- Point of care glucose monitoring may be unreliable in critically ill burn patients with low hemoglobin

Poster Presentation-SIS 2012

- Relationship between nasal swab *methicillin-resistant Staphylococcus aureus* (MRSA) PCR-positive test results and subsequent MRSA infection in thermal injury

Upcoming Presentations

Nasal MRSA-PCR in burn treatment algorithm

- To be presented at the 2012 ISBI

Projects Awaiting IRB Approval

- Rapid, Quantitative PCR-Based Detection of MRSA in Burn Sepsis Patients (a project with UC Davis funded by the ABA MCTG)
- A Retrospective Study Determining the Incidence and Treatment of Intra-abdominal Hypertension / Abdominal Compartment Syndrome in a Burn Treatment Center
- The Burn Experiences Study: Understanding the Recovery Process after Thermal Burn Injury (a project with UNC)
- A Comparison of the Nova Stat Strip Blood Glucose Testing System to the clinical laboratory blood glucose determinations with focus on hemoglobin levels

Projects Submitted and/or Accepted for Publication 2012

- Trimethoprim-induced hyperkalemia in burn admission treated with intravenous or oral trimethoprim sulfamethoxazole
- A Comparison of the Contour Blood Glucose Testing System to the Accu-Chek® Blood Glucose Testing System
- Retrospective Review of Inhalation Injury Patients Receiving APRV versus other Ventilator Modes for Respiratory Distress Syndrome or Acute Lung Injury in the Nathan Speare Regional Burn Treatment Center
- Elimination of resistant *Acinetobacter baumannii:* The success of a multidisciplinary task force
- Burn center management of operating room fires

The narrative below summarizes the project activities for Study 1 and Study 2 for each month of the project year, as documented in the project's quarterly reports:

July 2011

Study #1

52 screened. 52 excluded. 0 enrolled. 4 patients had TBSA >20%. 1 patient qualified, but no one in family spoke or read English. 2nd patient excluded due to age. 3rd patient with road rash excluded. 4th patient was admitted >24hrs post-burn.

Study #2

52 screened. 49 excluded. 3 enrolled. 3 completed.

August 2011

Study #1

57 screened. 52 excluded. 2 enrolled. 0 completed. 3 patients had TBSA >20%. 1st patient 25% TBSA, but didn't require central line. 2nd patient agreed to be in study and signed consent, but couldn't tolerate foley. 3rd patient enrolled & completed approx 44 hrs on DAQ before being transferred to another burn center.

Study #2

57 screened. 57 excluded. 0 enrolled. 0 completed. Several potential patients excluded due to psychiatric issues, road rash, and research staff not being aware of patient going to OR.

September 2011

Study #1

33 screened. 32 excluded. 1 enrolled. 1 completed. 2 patients had TBSA >20%. 1 patient excluded due to age (17 y/o).

Study #2

33 screened. 31 excluded. 2 enrolled. 0 completed. 1 patient removed due to issues with Aquacel Ag site, but followed for full study course. 1 patient didn't show up for follow-up appointments and was removed.

October 2011

Study #1

32 screened. 32 excluded. 0 enrolled. 0 completed. 1 patient had TBSA >20%, but was excluded due to extensive psych history, no CVC, and no foley.

Study #2

32 screened. 31 excluded. 1 enrolled. 1 completed.

November 2011

Study #1

26 screened. 25 excluded. 1 enrolled. 0 completed. 1 patient had TBSA >20%. Enrolled patient was only on system for 2-3 hours. Patient removed due to need for stat CT scan.

Study #2

26 screened. 26 excluded. 0 enrolled. 0 completed.

December 2011

Study #1

42 screened. 42 excluded. 0 enrolled. 0 completed. No patients had TBSA >20%.

Study #2

42 screened. 40 excluded. 2 enrolled. 1 completed. 1 patient was enrolled without viewing wounds prior to OR. Wounds assessed in OR and found to be 78cm^2 which is too small for the study.

January 2012

Study #1

47 screened. 47 excluded. 0 enrolled. 0 completed. 1 patient had TBSA >20%, but family was making patient a DNR. Patient expired within 36 hours of admission and potentially would have expired while in the study.

Study #2

47 screened. 46 excluded. 1 enrolled. 1 completed.

February 2012

Study #1

39 screened. 39 excluded. 0 enrolled. 0 completed. 4 patient had TBSA >20%. Of these 4 patients, 2 were <18 years old, 1 had no family available to give consent within first 24 hours, and 1 went to OR in first 24 hours after injury.

Study #2

39 screened. 39 excluded. 0 enrolled. 0 completed.

March 2012

Study #1

37 screened. 37 excluded. 0 enrolled. 0 completed. 1 patient had TBSA >20%. This patient went straight to OR on admission.

Study #2

37 screened. 36 excluded. 1 enrolled. 1 completed.

April 2012

Study #1

43 screened. 43 excluded. 0 enrolled. 0 completed. 2 patients had TBSA >20%. Of these 2 patients, 1 was excluded due to age <18 and the other was excluded because burn center staff did not notify the research team about the patient.

Study #2

43 screened. 43 excluded. 0 enrolled. 0 completed. 1 patient qualified, but research staff was not aware patient was going to OR.

May 2012

Study #1

53 screened. 52 excluded. 1 enrolled. 0 completed. 2 patients had TBSA>20%. 1 patient didn't require CVC until after 24 hour time frame. 1 patient enrolled, but data collection was interrupted due to computer malfunction. Army engineer contacted several times without response.

Study #2
53 screened. 53 excluded. 1 enrolled. 1 completed. Enrolled patient was scheduled for STSG. Patient went to OR, but only had excision and VAC placement.

June 2012
Study #1
51 screened. 51 excluded. 0 included. 0 completed. 1 patient had TBSA >20%, but didn't require CVC or foley within 24 hour time frame.
Study #2
51 screened. 49 excluded. 2 enrolled. 2 completed.

KEY RESEARCH ACCOMPLISHMENTS:

We have completed about 80% of our enrollment target for Study 2 (24/30) and continue to enroll patients. Study 1 commenced enrolling patients in April, 2011. 7 Patients have been enrolled with 3 patients completing the full 48 hours on the study. Data on the first 6 patients was submitted to the Army for analysis in March 2012.

REPORTABLE OUTCOMES:

For this report year, only 3 patients have fully completed Study 1. In the next report year, active transmission of data will continue and computer issues will be resolved. For Study 2, data will be entered into an Excel spreadsheet and validated. This data will be forwarded to the USAISR when 24 patients have completed the study. The Army will be responsible for statistical analysis of all data and for determining and reporting project outcomes.

CONCLUSION:

Conclusions will be drawn at the completion of the research projects.

REFERENCES:

No publications have been completed.

APPENDICES:

Not applicable.